JOSEPH ANTHONY FRANCISCO, Ph.D.
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PROFILE

Versatile Ph.D. scientist with over eight years of experience and proven leadership in developing protein therapeutics. Range of experience includes project team leadership, preclinical development, and protein/antibody engineering and development.

EDUCATION

Ph.D. in Chemical Engineering, The University of Texas at Austin, Austin, Texas, 1994.
Dissertation: The Expression of Recombinant Proteins on the External Surface of *Escherichia coli.*

B.A. in Chemical Engineering and Biochemistry, Rice University, Houston, Texas, 1989.

EXPERIENCE

Seattle Genetics, Inc., Bothell, WA (1998-present)
Director of Preclinical Development, (3/03-present)
Build and maintain a department (currently 1 Ph.D. and 5 Research Associates) responsible for internal and outsourced preclinical research and development. Responsibilities and accomplishments include:

- Establish a robust preclinical development process to move antibody-based product candidates from discovery into development.
- Establish departmental and team goals to meet project objectives and timelines.
- Serve as preclinical representative on Seattle Genetics priority projects.
- Participate on Priority team responsible for establishing corporate research and development priorities and making resource and budgetary recommendations to executive management.

Director of Molecular Development, (2001-2003)
Built multifunctional department responsible for preclinical development and protein/antibody engineering. Responsibilities and accomplishments include:

- Project team leader for SGN-30 program; entered Phase I clinical trials ahead of schedule and on budget in March 2002. Personal responsibilities included: oversight of contract development and GMP manufacturing; developing strategy for and implementing in house and outsourced pharmacology and toxicology studies; preparing pharmacology/toxicology section of IND; participating in preparation of CMC section of IND.
- Project team leader and preclinical sub team leader for SGN-17/SGN-19 program: lead Antibody-Directed Enzyme Prodrug Therapy. Responsible for maintaining communication and interaction with development partner Genencor International.

Associate Director of Molecular Biology, (2000-2001)
Conduct and supervise basic and applied research for the discovery and development of protein therapeutics for cancer. Responsibilities and accomplishments include:

- Direct research and development activities of molecular biology department.
- Establish and optimize antibody chimerization system, addressing relevant GMP issues.

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- Supervise *in vivo* pharmacology studies in relevant murine models.
- Selected as development project team leader for SGN-30 project; establish timelines, identify and assign personnel to key functions including contract manufacturing.

Principal Scientist, (1998-2000)
First Ph.D. research scientist to join Seattle Genetics. Directed a research program to investigate the therapeutic efficacy of novel antibodies and antibody-fusions as potential anti-cancer agents. Responsibilities and accomplishments include:
- Supervise the research activities of four associate scientists.
- Design and supervise preclinical studies to evaluate the toxicity and efficacy of numerous chemical and recombinant protein agents.
- Project team leader for SGN-14 program which was successfully outlicensed to a major biotech corporate partner.

Monsanto, St. Louis, MO (1997 - 1998)
Scientist, Protein Regulatory Sciences Department.
Responsible for the purification, characterization, and safety assessment of recombinant proteins expressed in plants for agricultural and pharmaceutical purposes. Duties included the design, implementation, and completion of studies and reports to support submissions to US and foreign agencies for regulatory approval.

Bristol-Myers Squibb Pharmaceutical Research Institute, Seattle, WA (1994 - 1997).
Research Investigator II, Molecular Immunology Department (1997).
Responsible for the construction and characterization of novel recombinant immunotoxins and antibodies for the treatment of cancer. Supervised the research activities of one research associate. Accomplishments include:
- Construction and *in vitro* and *in vivo* characterization of novel single-chain immunotoxins.
- Established the therapeutic efficacy of the antibodies to CD40 *in vitro* and in murine models of human lymphoma and multiple-myeloma.
- Member of the pre-IND project working group for a single-chain immunotoxin program.

Postdoctoral Fellow, Molecular Immunology Department (1994-1996).
Responsible for the engineering and characterization of single-chain immunotoxins targeted to CD40 and their evaluation as therapeutic agents for human lymphoma and multiple myeloma.

The University of Texas at Austin, Austin, TX (1989-1994).
Graduate Research Assistant, Department of Chemical Engineering. Supervised by Professor George Georgiou.
Responsible for designing, cloning, expressing and characterizing a novel protein fusion for the stable expression of recombinant proteins on the external surface of *E. coli*. (US Patent 5,348,867).
- Recipient of the Hoechst Celanese Corporation Graduate Presentation Award, 1993.
- Recipient of the Dow Centennial Fellowship, 1992.

PUBLICATIONS

Hamblett, H.J., Senter, P.D., Chace, D.F., Sun, M.M.C., Lenox, J., Cerveny, C.G., Kissler, K.M., Bernhardt, S.X., Kopcha, A.K., Zabinski, R.F., Meyer, D.L., and Francisco, J.A. Effects of drug loading on the antitumor activity of a monoclonal antibody drug conjugate, Clinical

Cancer Research, In Press

McDonagh, C.F., Beam, B.S., Wu, G.J.S., Chen, J.H., Chace, D.F., Senter, P.D., and Francisco, J.A. Improved yield and stability of L49-sFv-β-lactamase, a single-chain antibody fusion protein for anticancer prodrug activation, by protein engineering, Bioconjugate Chemistry, 14: 860-869, 2003.

Francisco, J.A., Cerveny, C.G., Meyer, D.L., Mixan, B.J., Klussman, K., Chace, D.F., Rejniak, S.X., Gordon, K., DeBlanc, R., Toki, B.E., Law, C.-L., Doronina, S.O., Siegall, C.B., Senter, P.D., and Wahl, A.F. cAC10-vcMMAE, an anti-CD30-monomethyl auristatin E conjugate with potent and selective antitumor activity, Blood, 102: 1458-1465, 2003.

Doronina, S.O., Toki, B.E., Torgov, M.Y., Mendelsohn, B.A., Cerveny, C.G., Chace, D.F., DeBlanc, R.L., Gearing, R.P., Siegall, C.B., Francisco, J.A., Wahl, A.F., Meyer, D.L., and Senter, P.D. Development of potent and highly efficacious monoclonal antibody auristatin conjugates for cancer therapy, Nature Biotechnology, 21: 778-784, 2003.

Wahl, A.F., Klussman, K., Thompson, J.D., Chen, J.H., Francisco, L.V., Risdon, G., Chase, D.F., Siegall, C.B., and Francisco, J.A. The anti-CD30 monoclonal antibody SGN-30 promotes growth arrest and DNA fragmentation *in vitro* and affects antitumor activity in models of Hodgkin's disease, Cancer Research, 62: 3736-3742, 2002.

Francisco, J.A., Donaldson, K.L., Chace, D., Siegall, C.B., and Wahl, A.F. Agonistic properties and *in vivo* antitumor activity of the anti-CD40 antibody SGN-14, Cancer Research, 60: 3225-3231, 2000.

Francisco, J.A. and Siegall, C.B. Single-chain immunotoxins targeted to CD40 for the treatment of human B-lineage hematologic malignancies, Leukemia and Lymphoma, 30: 237-245, 1998.

Francisco, J.A., Gawlak, S.L., Miller, M., Bathe, J., Russell, D., Chace, D., Mixan, B., Zhao, L., Fell, H.P., and Siegall, C.B. Expression and characterization of Bryodin 1 and a Bryodin 1-based single-chain immunotoxin from tobacco cell culture, Bioconjugate Chemistry, 8: 708-713, 1997.

Ledbetter, J.A., Francisco, J.A., Siegall, C.B., Gilliland, L.K., Hollenbaugh, D., Aruffo, A., Siadak, A.W., Mischel-Petty, N., Grosmaire, L.S., Gordon, M.L., Brown, T.J., Moran-Davis, P., Mittler, R.S., Kiener, P.K., and Nadler, S.G. Agonistic activity of a CD40 specific single-chain Fv constructed from the variable regions of mAb G28-5, Critical Reviews in Immunology, 17: 427-435, 1997.

Francisco, J.A., Gawlak, S.L., and Siegall, C.B. Construction, expression and characterization of BD1-G28-5 sFv, a single-chain anti-CD40 immunotoxin containing the ribosome-inactivating protein bryodin 1, Journal of Biological Chemistry, 272: 24165-24169, 1997.

Francisco, J.A., Schreiber, G.J., Comereski, C.R., Mezza, L.W., Warner, G.L., Davidson, T.J., Ledbetter, J.A., and Siegall, C.B. *In vivo* efficacy and toxicity of a single-chain immunotoxin

targeted to CD40, Blood, 89: 4493-4500, 1997.

Francisco, J.A., Kiener, P.A., Ledbetter, J.A., and Siegall, C.B. Cytokine activation sensitizes human monocytic and endothelial cells to the cytotoxic effects of an anti-CD40 immunotoxin, Journal of Immunology, 157: 1652-1658, 1996.

Francisco, J.A., Gilliland, L.K., Stebbins, M.R., Norris, N.A., Ledbetter, J.A., and Siegall, C.B. Activity of a single-chain immunotoxin that selectively kills lymphoma and other B-lineage cells expressing the CD40 antigen, Cancer Research 55: 3099-3104, 1995.

Francisco, J.A. and Georgiou, G. The expression of recombinant proteins on the external surface of *Escherichia coli*: biotechnological applications, Biochemical Engineering VIII: Annals of the New York Academy of Sciences, 372-382, 1994.

Georgiou, G., Poetschke, H.L., Stathopoulos, C., and Francisco, J.A. Practical applications of engineering Gram-negative bacterial cell surfaces, Trends in Biotechnology, 11: 6-10, 1993.

Francisco, J.A., Campbell, R., Iverson, B.L., and Georgiou, G. Production and fluorescence activated cell sorting of *Escherichia coli* expressing a functional antibody fragment on the external surface, Proceedings of the National Academy or Science, USA, 90: 10444-10448, 1993.

Francisco, J.A., Stathopoulos, C., Warren, R.A.J., Kilburn, D.G., and Georgiou, G. Specific adhesion and hydrolysis of cellulose by intact *Escherichia coli* expressing surface anchored cellulase or cellulose binding domains, Bio/Technology, 11: 491-495, 1993.

Francisco, J.A., Earhart, C.F., and Georgiou, G. Transport and anchoring of β-lactamase to the external surface of *Escherichia coli*, Proceedings of the National Academy of Science, USA, 89: 2713-2717, 1992.

PATENTS

Georgiou, G., Francisco, J.A., and Earhart, C.F. Expression of Proteins on Bacterial Surface, US Patent 5,348,867 (1994).

Siegall, C.B., Wahl, A.F., Francisco, J.A., and Fell, H.P. Recombinant Anti-Cd40 Antibody And Uses Thereof, WO 00/75348

Francisco, J.A., Risdon, G., Wahl, A.F., and Siegall, C.B. Recombinant Anti-Cd30 Antibodies And Uses Thereof, WO 02/43661

PRESENTATIONS

Francisco, J.A., Cerveny, C.G., Meyer, D.L., Siegall, C., Senter, P.D., and Wahl, A.F. "SGN-35, an Anti-CD30 Antibody-Drug Conjugate with Potent Antitumor Activity," Annual Meeting of the AACR (2003)

Francisco, J.A. "Preclinical Pharmacology and Toxicology of SGN-30, a Chimeric Anti-CD30

Antibody for the Treatment of Hodgkin's Disease," Invited speaker for Sierra Biomedical Annual Symposium: Biotechnology-Derived Therapeutics: Pharmacology and Toxicology Perspectives in Nonclinical Development (2003)

Ratcliffe, C.F., Beam, K.S., Wu, G.J.S., Chen, J., Dunn, J., Senter, P.D., and Francisco, J.A. "Improved Yield and Stability of L49-sFv-b-Lactamase, a Single-Chain Antibody Fusion Protein for Anticancer Prodrug Activation, by Protein Engineering," IBC Antibody Engineering conference (2001)

Francisco, J.A. "Molecular biology and bioconjugates," Invited speaker for Chemistry, Biology and Applications of Bioconjugates, Short Course at the American Chemical Society annual meeting (2000)

Francisco, J.A. "Antibody-based cancer therapeutics: Single-chain immunotoxins targeted to CD40," Invited speaker for the NIH Training Program in Biotechnology, The University of Texas at Austin (1999)

Francisco, J.A. and Siegall, C.B. "Single-chain immunotoxins as cancer chemotherapeutic agents," Antibody-Based Therapeutics: Applications and Clinical Data (1997).

Francisco, J.A., Schreiber, G.J., Warner, G.L., Davidson, T.J., Ledbetter, J.A., and Siegall, C.B. "*In vitro* and *in vivo* activity of G28-5 sFv-PE40, a single-chain immunotoxin targeted to CD40," Annual Meeting of the AACR (1997).

Francisco, J.A., Kiener, P.A., Ledbetter, J.A., Schreiber, G.J., and Siegall, C.B. "*In vitro* and *in vivo* activity of a single-chain immunotoxin targeted to CD40," Annual Meeting of the AACR (1996).

Francisco, J.A., Schreiber, G.J., Kiener, P.A., Stebbins, M.R., Ledbetter, J.A., and Siegall, C.B. "Characterization of single-chain immunotoxins targeted to CD40: antitumor activity versus B-lineage lymphoma cells," Fourth International Symposium on Immunotoxins (1995).

Francisco, J.A., Gilliland, L., Stebbins, M., Ledbetter, J.A., and Siegall, C.B. "Construction and characterization of G28-5 sFv-PE40, and anti-B cell lymphoma immunotoxin," Bristol-Myers Squibb Pharmaceutical Research Institute Fifth Annual Scientific Poster Session (1994).

Francisco, J.A., Ayling, A., Poetschke, H.L., Earhart, C.F., and Georgiou, G. "Molecular characterization of proteins expressed on the external surface of *Escherichia coli*," Annual Meeting of the ACS (1993).

PROFESSIONAL AFFILIATIONS

Study Section member, NIH SBIR grant review committee, Cancer Drug Development and Therapeutics
Member of the American Association for the Advancement of Science
Member of the American Association for Cancer Research